

UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 02-192)

PATENT

1645

P#8

In the Application of:

Progulske-Fox, et al

Serial No.: 09/849,115

Filed: May 5, 2001

For: Methods and Compositions for
Angioproliferative Disorder Treatment



Art Unit: 1645

Examiner: To be assigned

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TRANSMITTAL LETTER

Asst. Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

In regard to the above identified application,

1. We are transmitting herewith the attached:
 - a) Information Disclosure Statement;
 - b) PTO Form 1449 and 47 cited references;
 - c) Return postcard
2. With respect to fees:
 - a) It is believed no fee is due at this time.
 - b) Please charge any underpayment or credit any overpayment our Deposit Account, No. 13-2490.
3. GENERAL AUTHORIZATION: Please charge any additional fees or credit overpayment to Deposit Account No. 13-2490. A duplicate copy of this sheet is enclosed.
4. CERTIFICATE OF MAILING UNDER 37 CFR § 1.8: The undersigned hereby certifies that this Transmittal Letter and the paper, as described in paragraph 1, are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Asst. Commissioner for Patents, Washington, D.C. 20231 on April 23, 2002.

Date: April 23, 2002

Respectfully submitted,

Lisa M.W. Hillman

Registration No. 43,673

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INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to the duty of disclosure provided by 35 C.F.R. § 1.56 and §§ 1.97-98, the applicants wish to make the following references of record in the above-identified application. Copies of the references are enclosed. Copies are also listed in the PTO-1449 form enclosed herewith. It is requested that the documents be given careful consideration and that they be cited of record in the prosecution history of the present application so that they will appear on the face of the patent issuing from the present application.

In the judgment of the undersigned, portions of the references may be material to the examination of the pending claims, however no such admission is intended. 37 C.F.R. 1.97 (h). The references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is indented as to the relative

importance of any portion of the references. This Statement is not a representation that the cited references have effective dates early enough to be “prior art” within the meaning of 35 U.S.C. sections 102 or 103.

CITED REFERENCES

U.S. Patent Documents

<u>Document Number</u>	<u>Date</u>	<u>Name</u>	<u>Class</u>	<u>Filing Date If appropriate</u>
5,824,791	10/20/98	Progulske-Fox, et al.	536	12/11/95
5,830,710	11/03/98	Progulske-Fox, et al.	435	12/09/94
6,031,072	02/29/00	Blaschuk, et al.	530	07/11/97
6,110,747	08/29/00	Blaschuk, et al.	436	12/29/98
6,169,071 B1	01/02/01	Blaschuk, et al.	514	12/23/97

Foreign Documents

<u>Document Number</u>	<u>Date</u>	<u>Name</u>	<u>Country</u>
WO 99/60984	12/02/99	Holaday, et al.	PCT

Other Documents

1. Eckhardt, et al., “*A phase I clinical and pharmacokinetic study of the angiogenesis inhibitor, tecogalan sodium*”, *Annals of Oncology* 7:419-496, 1996
2. Irie, et al., “*Inhibition of Attachment and Chemotactic Invasion of Uterine Endometrial Cancer Cells by a New Vinca Alkaloid, Conophylline*”, *Anticancer Research*, 19:3061-3066, 1999
3. Fidler, et al., “*The Implications of Angiogenesis for the Biology and Therapy of Cancer Metastasis*”, *Cell*, Vol. 79, 185-188, 1994
4. Stupack, et al., “*ECM Remodeling Regulates Angiogenesis: Endothelial Integrins Look for New Ligands*”, *Science's site*, p. 1-6, 2002
5. Chen, et al., “*A Strategy to Discover Circulating Angiogenesis Inhibitors Generated by Human Tumors*”, *Cancer Research*, 55:423-4233, 1995
6. O'Reilly, et al., “*Endostatin: An Endogenous Inhibitor of Angiogenesis and Tumor Growth*”, *Cell*, Vol. 88, p. 277-285, 1997

7. Yamaguchi, et al., "Endostatin inhibits VEGF-induced endothelial cell migration and tumor growth independently of zinc binding", *The EMBO Journal*, Vol. 18, pp. 4414-4423, 1999
8. Vitale, et al., "Apoptosis induced by denied adhesion to extracellular matrix *anoikis) in thyroid epithelial cells is p53 dependent but fails to correlate with modulation of p53 expression", *FEBS Letters* 462, pp. 57-60, 1999
9. Attwell, et al., "The integrin-linked kinase (ILK) suppresses anoikis", *Oncogene* 19(33):3811-15, 2002
10. Rosen, et al., "Activated ras Prevents Downregulation of Bcl-X_L Triggered by Detachment from the Extracellular Matrix: A Mechanism of ras-induced Resistance to Anoikis in Intestinal Epithelial Cells", *The Journal of Cell Biology*, Vol. 149, No. 2, pp. 447-455, 2000
11. Rytömaa, et al., "Involvement of FADD and caspase-8 signaling in detachment-induced apoptosis", *Current Biology*, Vol. 9, No. 18, pp. 1043-1046, 1999
12. Erdreich-Epstein, et al., "Integrins $\alpha\beta_3$ and $\alpha\beta_5$ are Expressed by Endothelium of High-Risk Neuroblastoma and Their Inhibition is Associated with Increased Endogenous Ceramide", *Cancer Research*, 60, 712-721, 2000
13. Lee, et al., " $\alpha 5\beta 1$ Integrin Protects Intestinal Epithelial Cells from Apoptosis through a Phosphatidylinositol 3-Kinase and Protein Kinase B-dependent Pathway", *Molecular Biology of the Cell*, Vol. 11, pp 1973-1987, 2000
14. Kawahara, et al., "Inhibitory effects of adhesion oligopeptides on the invasion of squamous carcinoma cells with special reference to implication of αv integrins", *J. Cancer Res. Clin. Oncol.*, 121:133-140, 1995
15. Ruoslahti, "Integrins as signaling molecules and targets for tumor therapy", *Kidney International*, Vol. 51, pp. 1413-1417, 1997
16. Brassard, et al., "Integrin $\alpha\beta_3$ -Mediated Activation of Apoptosis", *Experimental Cell Research* 251, pp. 33-45, 1999
17. Kottke, et al., "Comparison of Paclitaxel-, 5-Fluoro-2'-deoxyuridine-, and Epidermal Growth Factor (EGF)-induced Apoptosis", *The Journal of Biological Chemistry*, Vol. 274, No. 22, pp. 15927-15936, 1999
18. Dark, et al., "Combretastain A-4, an Agent that Displays Potent and Selective Toxicity toward Tumor Vasculature", *Cancer Res.*, Vol. 57, pp. 1829-1834, 1997

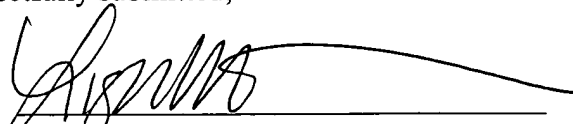
19. Taddei, et al., "Inhibitory Effect of Full-Length Human Endostatin on *in Vitro* Angiogenesis", *Biochemical and Biophysical Research Communications*, 263, pp. 340-345, 1999
20. Albini, et al., "Somatostatin controls Kaposi's sarcoma tumor growth through inhibition of angiogenesis", *The FASEB Journal*, Vol. 13, pp. 647-655, 1999
21. Stack, et al., "Angiostatin inhibits endothelial and melanoma cellular invasion by blocking matrix-enhanced plasminogen activation", *Biochem. J.*, 340, pp. 77-84, 1999
22. Layman, "Angiosuppressive Protein from *P. Gingivalis*", Abstract
23. Paramaesvaran, et al., "Vascular disruption by a 15kDa adhesin domain from *Porphyromonas gingivalis*", *J. Dental Res.*, 77:664, 1998
24. Phillips, et al., "Alterations in cell morphology and cytoskeletal proteins in gingival fibroblasts exposed to a *Bacteroides gingivalis* extract", *J. Periodont. Res.*, 25:339-346, 1990
25. Baba, et al., "Anti-angiogenesis agent DS-4152 is a potent and selective inhibitor of HIV-1 replication *in vitro*", *AIDS*, Vol. 8, No. 1, pp.43-48, 1994
26. Wu, et al., "*Bacteroides fragilis* enterotoxin cleaves the zonula adherens protein, E-cadherin", *Proc. Natl. Acad. Sci. USA*, Vol. 95, pp. 14979-14984, 1998
27. Hecht, et al., "Clostridium difficile Toxin A Perturbs Cytoskeletal Structure and Tight Junction Permeability of Cultured Human Intestinal Epithelial Monolayers", *J. Clin. Invest.*, Vol. 82, pp. 1516-1524, 1988
28. Wan, et al., "Der p 1 facilitates transepithelial allergen delivery by disruption of tight junctions", *The Journal of Clinical Investigation*, Vol. 104, No. 1, pp. 123-133, 1999
29. Haapasalo, et al., "Degradation of basement membrane collagen by proteases from some anaerobic oral microorganisms", *Oral Microbiol. Immunol.*, 3:97-102, 1988
30. Smalley, et al., "The degradation of type I collagen and human plasma fibronectin by the trypsin-like enzyme and extracellular membrane vesicles of *Bacteroides Gingivalis* W50", *J. Arch. Oral Biol.*, Vol. 33 (5), pp. 323-329, 1988
31. Shah, et al., "Assessment of the Relative Cytotoxicity of *Porphyromonas gingivalis* Cells, Products, and Components on Human Epithelial Cell Lines", *J. Periodontol.*, Vol. 63, No. 1, pp. 44-51, 1992

32. Mizejewski, "Role of Integrins in Cancer: Survey of Expression Patterns", *Integrins Expression in Cancer*, Vol. 222, pp. 124-138, 1999
33. Velasco-Velazquez, et al., "Integrins and integrin-associated molecules: Targets for the development of antimetastatic therapies", *Rev. Invest. Clin.*, 51(3):183-93, 1999
34. Scragg, et al., "Targeted disruption of Fibronectin-Integrin Interactions in Human Gingival Fibroblasts by the RI Protease of *Porphyromonas gingivalis* W50", *Infection and Immunity*, Vol. 67, No. 4, pp. 1837-1843, 1999
35. Johansson, et al., "Characterization of the proteinase-dependent cytotoxicity of *Porphyromonas gingivalis*", *Eur. J. Oral Sci.*, 106, pp. 863-871, 1998
36. Katz, et al., "Characterization of *Porphyromonas gingivalis*-Induced Degradation of Epithelial Cell Junctional Complexes", *Infection and Immunity*, Vol. 68, No. 3, pp. 1441-1449, 2000
37. Chen, et al., "Protease-Active Extracellular Protein Preparations from *Porphyromonas gingivalis* W83 Induce N-Cadherin Proteolysis, Loss of Cell Adhesion, and Apoptosis in Human Epithelial Cells", *J. Periodontol.*, Vol. 72, No. 5, pp. 641-650, 2001
38. Layman, et al., "Suppression of Fibroblast Growth by *Bacteroides gingivalis* Endotoxin is not Reduced by Serum Lipoproteins", *J. Periodontol.*, Vol. 60, No. 5, pp. 259-263, 1989
39. Layman, et al., "Growth Inhibitory Effects of Endotoxins from *Bacteroides gingivalis* and *intermedius* on Human Gingival Fibroblasts in vitro", *J. Periodontol.*, Vol. 58, No. 6, pp. 387-392, 1987
40. Chen, et al., "Cleavage of N-Cadherin by extracellular proteases from *Porphyromonas gingivalis*", *J. Dent. Res.*, 79 (IADR Abstracts), Abstract No. 706, 2000
41. Josephson, *Biological Solvent for Killing Tumors*, *Mod. Drug Disc.*, p. 16, March 2000

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